Cell Biology (or Biology or Molecular Biology)

EFFECT OF CADMIUM AND OSTEOPONTIN ON RHO-A AND THE ACTIN CYTOSKELETON IN OSTEOCLASTS

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At low concentrations, cadmium exposure has been linked to bone loss. Cadmium affects osteoclasts, the bone resorbing cells, at these concentrations. Our previous research indicated that cadmium may be acting via Rho-A GTPase, a small signaling molecule that is responsible for the formation and maintenance of stress fibers and temporary focal adhesion plaques called podosomes. Osteopontin is an extracellular matrix protein containing an RGD sequence that causes an increase in stress fibers, podosome number and actin ring formation. Like cadmium, it increases osteoclast motility and bone resorption. RhoA plays a role in osteopontin-induced signal transduction and cytoskeletal reorganization. To determine if cadmium was causing an effect similar to osteopontin, osteoclasts were differentiated *in vitro* using mouse bone marrow cells cultured with RANKL and M-CSF. A time course for cadmium or osteopontin exposure was performed. The cells were immunohistochemically stained for Rho-A, which was visualized with an Alexa Fluor 488 secondary antibody. F-actin was visualized by staining with Alexa Fluor 588 labeled phalloidin. In the osteopontin treated cells, more stress fibers were observed along with distinct podosomes at various positions in the cell center. Cadmium treated cells also displayed more stress fibers than in the controls but these fibers were not as regular as with osteopontin. After 60 minutes of cadmium exposure, the actin cytoskeleton was much more disorganized throughout the cell. The Rho-A staining was located towards the center in all cells. These data suggest that although cadmium may be working via Rho A, the result on the actin cytoskeleton is not the same as for osteopontin.